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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

To:

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Date of mailing
(day/month/year)

23.09.2004

Applicant's or agent's file reference
PB-46676

IMPORTANT NOTIFICATION

International application No.
PCT/GB 03/03654

International filing date (day/month/year)
20.08.2003

Priority date (day/month/year)
21.08.2002

Applicant
PHOQUS PHARMACEUTICALS LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

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|---------|----|----------|
| PARTNER | PB | FILE NO. |
| TA | | 46676 |
| RECORDS | PD | |

Name and mailing address of the International preliminary examining authority:



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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference PB-46676 | | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416) | |
| International application No. PCT/GB 03/03654 | International filing date (day/month/year) 20.08.2003 | Priority date (day/month/year) 21.08.2002 | |
| International Patent Classification (IPC) or both national classification and IPC A61K9/16 | | | |
| Applicant PHOQUS PHARMACEUTICALS LIMITED et al. | | | |

| | |
|---|--|
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 1 sheets.</p> | |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> | |

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|---|--|
| Date of submission of the demand 27.02.2004 | Date of completion of this report 23.09.2004 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Sindel, U Telephone No. +49 89 2399-7064  |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/GB 03/03654**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-25 as originally filed

Claims, Numbers

7-28 as originally filed

1-6 filed with telefax on 14.09.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/GB 03/03654**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-28 |
| | No: Claims | - |
| Inventive step (IS) | Yes: Claims | 1-28 |
| | No: Claims | - |
| Industrial applicability (IA) | Yes: Claims | 1-28 |
| | No: Claims | - |

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB 03/03654

Reference is made to the following document:

D1: EP 1 116 485

The Applicant is informed that there exists an intermediate document which might become relevant in the European Phase of the application. The intermediate document is WO 03/072084 having a priority of 28.02.2002, a date of filing of 28.02.2003 and a publication date of 4.09.2003.

Item V

1) Novelty

The subject-matter of claims 1-28 is new in the sense of Article 33(2) PCT in view of the prior art.

2) Inventive step

The subject-matter of claims 1-28 involves an inventive step in the sense of Article 33(3) PCT in view of the prior art.

The problem to be solved was the stickiness during tableting of granules being made with an aqueous solution of citric acid as granulation liquid.

The solution provided is the addition of a water-soluble sugar like lactitol to the granulation liquid.

Closest prior art is D1 describing the use of an aqueous solution of sucrose and citric acid as granulation liquid for the production of instant granules (see example 1). The granulate is used directly as such without any additional tableting step. Hence, the problem of stickiness during tableting - which was solved with the present application - does not occur.

3) Industrial applicability

The subject-matter of claims 1-28 is industrially applicable in the sense of Article 33(4) PCT.

CLAIMS

1. The use of a highly water-soluble sugar in an aqueous solution of citric acid as a binder for the granulation of tablet excipients to reduce the sticking of the tablet excipients when subject to compression.

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2. The use as claimed in Claim 1 in which the highly water-soluble sugar is based on simple crystalline C5 or C6 sugar structures and is a mono-, di, tri or polysaccharide with a degree of polymerisation of less than 20, preferably less than 10.

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3. The use as claimed in Claim 2 in which the highly water-soluble sugar is selected from glucose, sucrose, maltose, lactose, arabinose, xylose, ribose, fructose, mannose, galactose, sorbose, trehalose, sorbitol, xylitol, mannitol, maltitol, lactitol, isomaltol, maltodextrin, hydrogenated starch hydrolysed

15 products and mixtures thereof.

4. The use as claimed in Claim 3 in which the sugar is selected from maltitol, lactitol, sucrose, trehalose and mixtures thereof.

20 5. The use as claimed in any preceding claim in which the weight ratio of citric acid to highly water-soluble sugar is from 1:10 to 10:1.

6. The use as claimed in Claim 5 in which the weight ratio of citric acid to highly water-soluble sugar is from 2:10 to 10:2, preferably 5:10 to 10:5.

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